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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/576,372

04/19/2006

Mara Rossi

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EXAMINER

DANG, IAN D

ART UNIT

PAPER NUMBER

1647

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DELIVERY MODE

10/09/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/576,372	<b>Applicant(s)</b> ROSSI ET AL.	
	<b>Examiner</b> Ian Dang	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 22-45 is/are pending in the application.
- 4a) Of the above claim(s) 26-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-25 and 32-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 22-45 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>04/19/2006</u> | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of the species ion exchange chromatography in the reply filed on 09/14/2007 is acknowledged.

The traversal is on the ground that the claims are all linked by a special technical feature that involves the use of hydrophobic charge induction chromatography in the process for the production of purified IL-18 BP. In addition, Applicant argues that the different structural and functional features of chromatography resins are insufficient for a finding that the presently claimed invention lack unity.

Applicant's arguments have been fully considered but are not found persuasive. As disclosed in the Office action mailed 8/14/2007, the species listed in claims 24 and 25 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the chromatography resins listed in claims 24 and 25 do not share common structural and functional features. Each type of chromatography resin separates proteins based on specific protein characteristics. In addition, the hydrophobic charge induction chromatography is a single step in the process for the purification of IL-18BP. Additional subsequent steps with different types of chromatography are also needed for the purification of IL-18BP. Under PCR Rule 13.1, the application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

It is noted that each species listed in the previous Office action is independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required.

The requirement is still deemed proper and is therefore made FINAL.

***Status of Application, Amendments and/or Claims***

The amendment of 19 April 2006 has been entered in full. Claims 1-21 have been cancelled and claims 22-45 have been added. Claims 29-31 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 09/14/2007.

Claims 22-25, 27-28 and 32-45 are pending and under examination.

***Claim Objections***

Claims 22 is objected to because of the following informalities:

Claim 22 uses an acronym without first defining what it represents in the independent claims (see for example, "IL-18BP"). While the claims can reference acronyms, the material presented by the acronym must be clearly set forth at the first use of the acronym.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112 (Second Paragraph)***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1647

Claims 22-25, 27-28 and 32-42, 44-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "fluid" in claims 22, 24, and 43, is a relative term which renders the claims 22-25, 27-28 and 32-42, 44-45 indefinite. The term "fluid" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, it is not clear what type of fluid is loaded onto a hydrophobic charge-induction chromatography resin. Is the fluid recited in the claim blood or cell lysate?

Claims 32, 34, and 36 are rejected as being indefinite because it is unclear how the limitations of claim 32 relate to claim 22. The recitation of claim 32 does not provide any indication regarding how the steps disclosed in the claim relate to the process for the production of purified IL-18BP comprising the hydrophobic charge-induction chromatography disclosed in claim 22. For example, do the steps in claim 32 occur after the steps in claim 22? Or, before the steps in claim 22? Which steps are required for the purification of IL-18BP?

The phrase "virus removal filtration steps" in claims 35-37 is a relative phrase which renders the claims 35-37 indefinite. The phrase "virus removal filtration steps" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what the purification steps encompasses the removal of virus by filtration steps.

Claims 44-45 are rejected as being indefinite because it is unclear how the limitations of claim 44 relate to claim 22. The recitation of claim 44 does not provide any indication regarding how the steps disclosed in the claim relate to the process for the production of purified IL-18BP

Art Unit: 1647

comprising the hydrophobic charge-induction chromatography disclosed in claim 22. For example, do the steps in claim 44 occur after the steps in claim 22? Or, before the steps in claim 22? Which steps are required for the purification of IL-18BP?

The term "strong anion exchange chromatography" in claim 39 is a relative term which renders the claim 39 indefinite. The term "strong anion exchange chromatography" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, how does strong anion exchange chromatography relate to anion exchange chromatography?

***Claim Rejections - 35 USC § 112 (Written Description)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-25, 27-28 and 32-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 22 is drawn to a process for the production of purified interleukin-18 binding protein (IL-18BP). Claims 35-37 are drawn to one or more virus.

The specification teaches that four isoforms of IL-18BP generated by alternative mRNA splicing have been identified in humans so far. They were designated IL-18BP a, b, c, and d, all

Art Unit: 1647

sharing the same N-terminus and differing in the C-terminus (Novick et al. 1999). These isoforms vary in their ability to bind IL-18 (Kim et al. 2000). Of the four human IL-18BP (hIL-18BP) isoforms, isoforms a and c are known to have a neutralizing capacity for IL-18. The most abundant IL-18BP isoform, isoform a, exhibits a high affinity for IL-18 with a rapid on-rate and a slow off-rate, and a dissociation constant ( $K_d$ ) of approximately 0.4 nM (Kim et al. 2000) (page 5, lines 4-10). In addition, IM et al., (2002, Journal of Interferon and cytokine Research, Volume 22, pages 321-328) teach the cloning, expression and characterization of rat interleukin binding protein (abstract). Finally, the specification does not provide any teachings regarding the virus required for the purification of IL-18 BP.

Thus, the claim is genus claims. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Specifically, the specification does not clearly define interleukin-18 binding protein (IL-18BP), a virus and all methods of using such. Thus, the scope of the claims includes numerous structural and functional variants, and the genus' are highly variant because a significant number of structural and functional differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural and functional features that could distinguish interleukin-18 binding protein (IL-18BP) and a virus are missing from the disclosure. No common attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, interleukin-18 binding protein (IL-18BP) and a virus are insufficient to describe the genus.

The written description requirement for a claimed genus' may be satisfied through sufficient description of a representative number of species by actual reduction to practice,

Art Unit: 1647

reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus for interleukin-18 binding protein (IL-18BP), a virus, and all methods of using such.

There is no description of the special features, which are critical to the structure and function of the genus claimed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify interleukin-18 binding protein (IL-18BP) and a virus encompassed by the claims. Thus, no identifying characteristics or properties of the instant interleukin-18 binding protein (IL-18BP) and virus are provided such that one of skill would be able to predictably identify the encompassed variant biological and chemical entities recited in the methods of the instant claims. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors.

In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-25, 27-28, 38, 39, 42, 43, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boschetti E. (2002, TRENDS in Biotechnology, Volume 20, Issue 8, pages 333-337) in view of Xiang et al. (2001, The Journal of Biological Chemistry, Volume 276, Issue 20, pages 17380-17386).

Boschetti E. (2002, TRENDS in Biotechnology, Volume 20, Issue 8, pages 333-337) teaches that hydrophobic charge induction chromatography using 4-mercapto-ethyl-pyridine as the ligand is an effective method for the separation of antibodies from a variety of feedstocks (page 333, abstract). In addition, Boschetti E. teaches that to reach the high purity required for therapeutic applications, the combination of two or more chromatographic procedures is necessary (page 336, right column 3<sup>rd</sup> full paragraph). Moreover, Boschetti E. teaches that the aim of the first capture step is to selectively adsorb antibodies (page 336, right column 3<sup>rd</sup> full paragraph). Furthermore, Boschetti E. teaches that several suggestions can be formulated for the use of HCIC in combination with complementary separation techniques, such as the combination of HCIC with anion exchange or with hydroxyapatite chromatography (page 336, right column 3<sup>rd</sup> full paragraph). Finally, Boschetti E. teaches that cation exchange capture step

Art Unit: 1647

be followed by HCIC (page 336, right column, end of 3<sup>rd</sup> full paragraph). However, Boschetti does not teach a process for the purification of IL-18BP.

Xiang et al. (2001, The Journal of Biological Chemistry, Volume 276, Issue 20, pages 17380-17386) teach that approximately 60% of the mature human IL-18BP resembles an immunoglobulin (Ig) domain that includes a highly conserved pair of cysteines and tryptophan residues (page 17380, right column, 1<sup>st</sup> full paragraph). In addition, Xiang et al. teach that IL-18BP was purified from cell culture supernatant (page 17381, left column 2<sup>nd</sup> full paragraph).

Thus, it would be obvious for one skilled in the art to modify the hydrophobic charge induction chromatography purification process as taught by Boschetti E. (2002) by utilizing it for the purification of IL-18BP in view of Xiang et al. (2001). One of ordinary skill in the art at the time the invention was made would be motivated to modify the method for the purification of IL-18BP because the hydrophobic charge induction chromatography (HCIC) represents an improvement towards achieving the ideal situation in the design of an antibody-selective sorbent and the operating characteristics of the sorbents permits significant process simplification compared with traditional approaches, and also a good level of specificity (Boschetti et al., 2002, page 333, right column 2<sup>nd</sup> full paragraph). One skilled in the art would have expected success because methods of purifying antibodies with by utilizing HCIC were available and practiced at the time the invention was made. Accordingly, the invention taken as a whole is *prima facie* obvious.

### **Conclusion**

No claim is allowed.

Art Unit: 1647

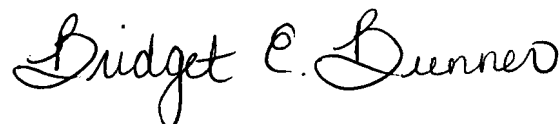
### Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang  
Patent Examiner  
Art Unit 1647  
September 28, 2007



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